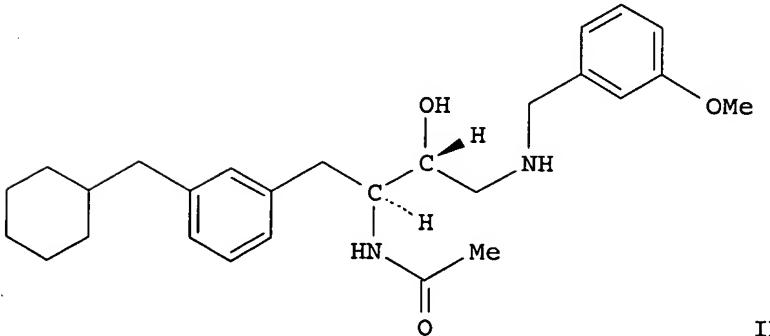
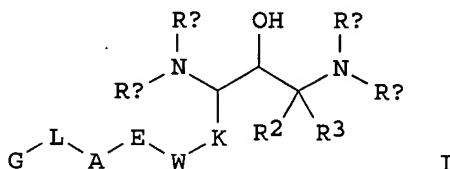


1/19/2005

ANSWER 6 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2003:472477 CAPLUS
 DOCUMENT NUMBER: 139:52753
 TITLE: Preparation of substituted hydroxyethylamines as
 β -secretase inhibitors
 INVENTOR(S): Tenbrink, Ruth; Maillard, Michel; Warpehoski, Martha
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
 Company
 SOURCE: PCT Int. Appl., 306 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050073	A1	20030619	WO 2002-US39050	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004044072	A1	20040304	US 2002-313849	20021206
EP 1453788	A1	20040908	EP 2002-795769	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014736	A	20041123	BR 2002-14736	20021206
PRIORITY APPLN. INFO.:			US 2001-338452P	P 20011206
			WO 2002-US39050	W 20021206

OTHER SOURCE(S): MARPAT 139:52753
 GI



AB Title compds. I [E = bond, alkylene; RA = H, benzyloxycarbonyl; RD = H, alkoxy carbonyl; K = (un)substituted alkyl; A = aryl, cycloalkyl, heteroaryl, etc.; W = bond, SOO-2, (un)substituted amino; L = bond, absent, etc.; G = absent, alkyl, cycloalkyl, etc.; R2-3 = H, alkyl, aryl, etc.; RN = Ph naphthyl, tetralinyl, etc.; RC = heteroaryl, etc.] are prepared as β -secretase inhibitors. For instance, N-[(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl] acetamide (II) isolated as the HCl salt is prepared in several steps. The key intermediate in the synthesis is derived from the asym. hydrogenation of Me 2-[(benzyloxy)carbonyl]amino]-3-(2-bromophenyl)acrylate (preparation given) to give the corresponding phenylalanine analog intermediate. I are useful for the treatment of Alzheimer's disease.

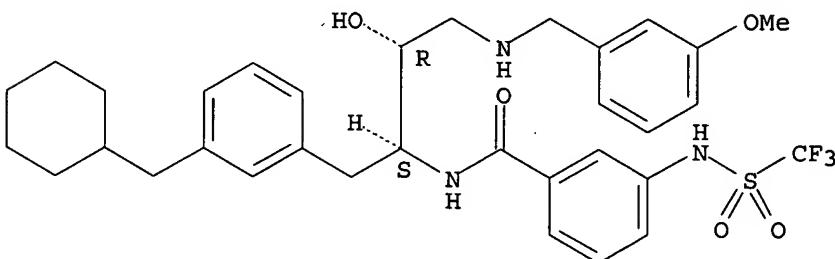
IT 527722-73-2P 527722-74-3P 546115-09-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted hydroxyethylamines as β -secretase inhibitors)

RN 527722-73-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3-(cyclohexylmethyl)phenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-3-[(trifluoromethyl)sulfonyl]amino] - (9CI) (CA INDEX NAME)

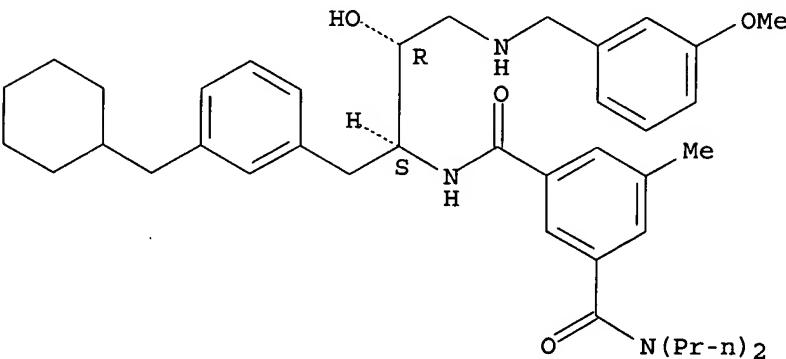
Absolute stereochemistry.



RN 527722-74-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-(1S,2R)-1-[(3-(cyclohexylmethyl)phenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl - (9CI) (CA INDEX NAME)

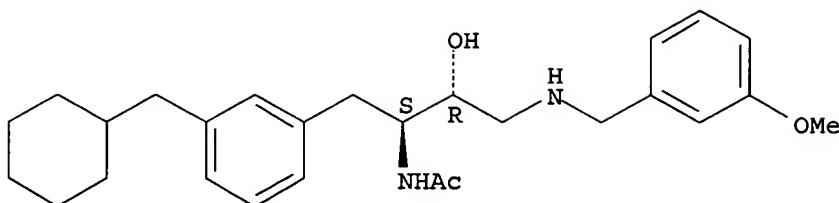
Absolute stereochemistry.



RN 546115-09-7 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[(3-(cyclohexylmethyl)phenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 527730-33-2P 527730-41-2P 527730-58-1P
527731-12-0P 527731-44-8P 546115-10-0P
546115-11-1P 546115-12-2P 546115-13-3P
546115-14-4P 546115-15-5P 546115-23-5P
546115-24-6P 546115-25-7P 546115-26-8P
546115-27-9P 546115-28-0P 546115-29-1P
546115-30-4P 546115-31-5P 546115-32-6P

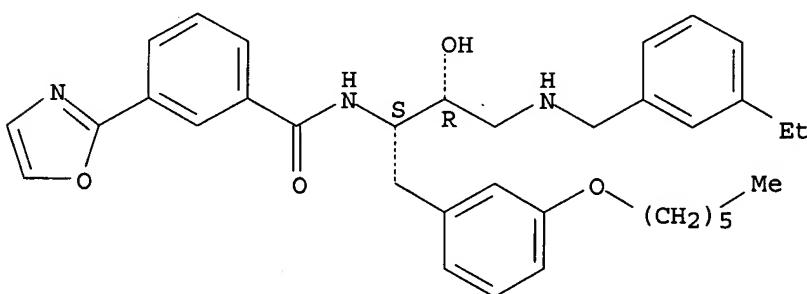
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted hydroxyethylamines as β -secretase inhibitors)

RN 527730-33-2 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[3-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

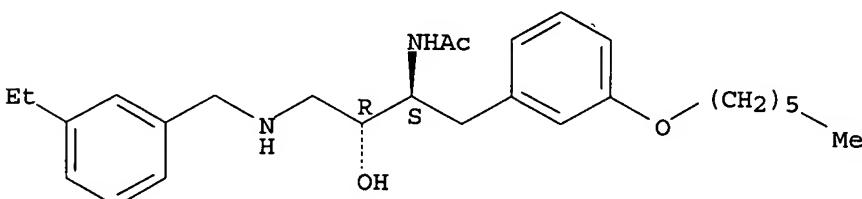
Absolute stereochemistry.



RN 527730-41-2 CAPLUS

CN Acetamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[3-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

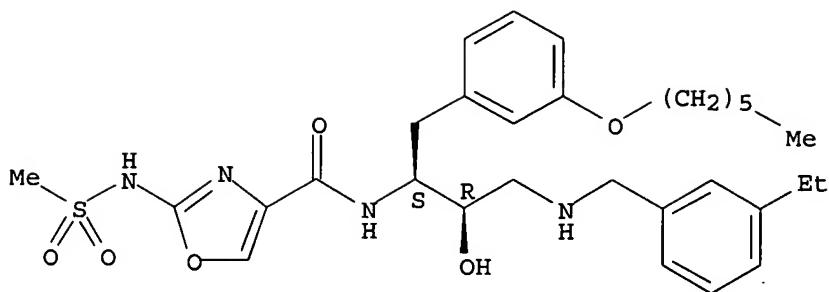
Absolute stereochemistry.



RN 527730-58-1 CAPLUS

CN 4-Oxazolecarboxamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[3-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

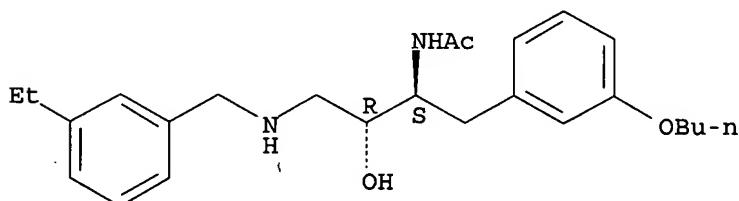
Absolute stereochemistry.



RN 527731-12-0 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[(3-butoxyphenyl)methyl]-3-[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

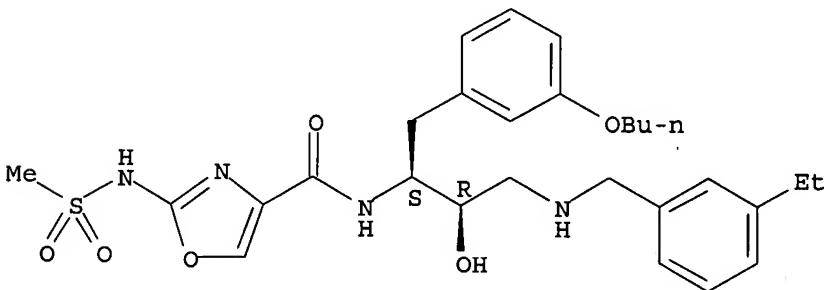
Absolute stereochemistry.



RN 527731-44-8 CAPLUS

CN 4-Oxazolecarboxamide, N-[(1S,2R)-1-[(3-butoxyphenyl)methyl]-3-[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

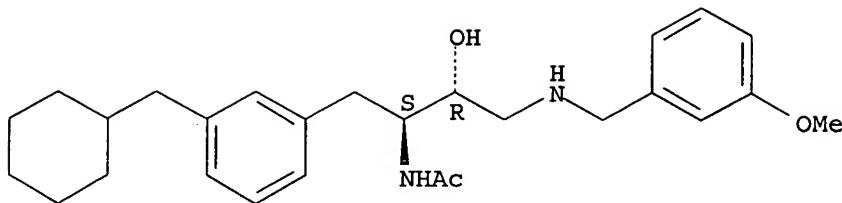
Absolute stereochemistry.



RN 546115-10-0 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

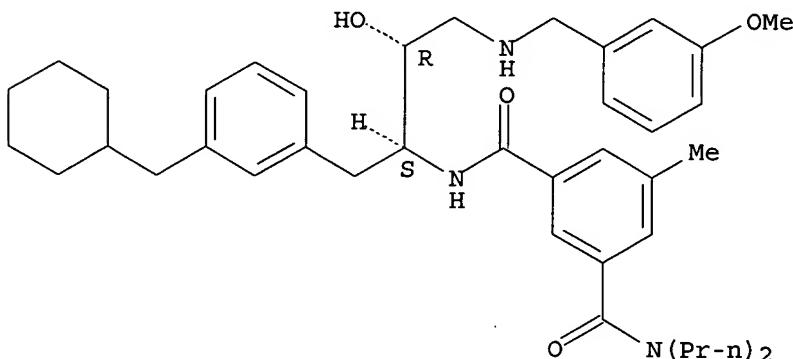


● HCl

RN 546115-11-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-(1S,2R)-1-[(3-(cyclohexylmethyl)phenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

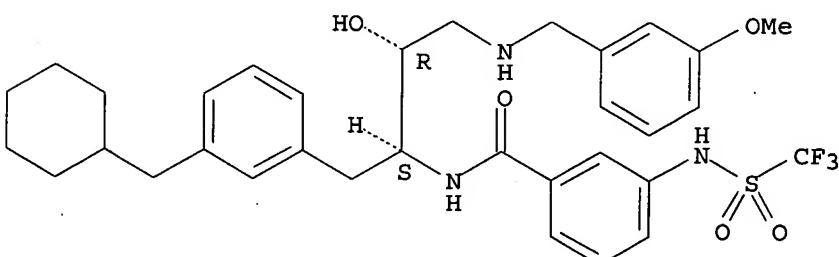


● HCl

RN 546115-12-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3-(cyclohexylmethyl)phenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-3-[(trifluoromethyl)sulfonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl